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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/570,010	02/27/2006	Cynthia C. Bamdad	13150-70089US	8164

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EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	PAPER NUMBER
1643	
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09/19/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/570,010	BAMDAD, CYNTHIA C.	
	Examiner	Art Unit	
	LYNN BRISTOL	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1,13,14,17,27,57-62 and 196-199* is/are pending in the application.

5a) Of the above claim(s) *27 and 57-62* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1,13,14,17 and 196-199* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/10/11 and 8/10/11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 13, 14, 17, 27, 57-62 and 196-199 are all the pending claims for this application.

2. Claims 27 and 57-62 are withdrawn from further consideration pursuant to 37 CFR 1.142(b).

3. The amendment to the specification of 7/5/11 has been entered.

4. Claims 1, 13, 14, 17 and 196-199 are all the pending claims under examination.

5. This office action is final.

Information Disclosure Statement

6. The IDS' of 8/10/11 and 8/10/11 have been considered and entered. The initialed and signed 1449 forms are attached. The WO 03/054154 reference on the 1449 form has been stricken. Applicants have not provided a complete copy of the foreign reference document.

Withdrawal of Rejections

Claim Rejections - 35 USC § 102

7. The rejection of Claims 1, 13, 14, 17 and 196-199 under 35 U.S.C. 102(e) as being anticipated by Bamdad et al. (US 20030036199; published February 20, 2003; filed November 27, 2001; cited in the PTO 892 form of 8/22/07) is withdrawn.

Applicants petition to claim benefit of priority to the same filing date of Bamdad et al. (US 20030036199) has been granted by the Petitions Branch. The priority document,

09/996,069, has been confirmed by the examiner to contain the disclosure for antibodies to the PSMGFR protein having the sequence GTINVHDVETQFNQYKTEAASPYNLTISDVSVSDVPFPF SAQSGA and which is identical to instant claimed SEQ ID NO: 36. The instant claims are entitled benefit to the prior-filed applications.

Claim Rejections - 35 USC § 103

8. The rejection of Claims 1 and 17 (and new Claims 196 and 199) under 35 U.S.C. 103(a) as being unpatentable over Kufe et al. (WO 02/22685; published 3/21/02; filed 12/11/01; cited in the PTO 892 form of 1/31/08) in view of Bamdad et al. (US 20030036199; published February 20, 2003; filed November 27, 2001; cited in the PTO 892 form of 8/22/07) is withdrawn.

Applicants petition to claim benefit of priority to the same filing date of Bamdad et al. (US 20030036199) has been granted by the Petitions Branch. The priority document, 09/996,069, has been confirmed by the examiner to contain the disclosure for antibodies to the PSMGFR protein having the sequence GTINVHDVETQFNQYKTEAASPYNLTISDVSVSDVPFPF SAQSGA and which is identical to instant claimed SEQ ID NO: 36. The instant claims are entitled benefit to the prior-filed applications.

Rejections Maintained

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

9. The rejection of Claims 1, 13, 14, 196, 197 and 198 under 35 U.S.C. 102(e) as being anticipated by Wreschner et al. (US 20050019324; published 1/27/05; filed 3/26/02; cited in the PTO 892 form of 1/31/08) is maintained.

The rejection was maintained in the Office Action of 10/31/08 as follows:

"Applicants' allegations on p. 9 of the Response of 7/31/08 have been considered but are not found persuasive. Applicants allege "Wreschner discloses a monoclonal antibody (BOS7D10) against MUC1 that inhibits cell growth. However, the disclosed antibody appears to be a bi-valent antibody. Since Wreschner is silent as to the anti-cell proliferation effects of the monovalent antibody over bivalent antibody, the presently claimed monovalent antibody is distinguished over the bivalent antibody described in Wreschner."

Response to Arguments

Wreschner discloses an isolated antibody or fragment including monovalent and bivalent antibodies and fragments [0034; 0047], which specifically binds to an epitope in the extracellular region of an isoform of MUC1 protein [0019] where the epitope is located in the 15 amino acid sequence that resides at the N-terminal portion of the 59 amino acid segment which is located directly N-terminal to the transmembrane domain of the MUC1/Y, MUC1/X and MUC1/REP proteins [0044], a pharmaceutical composition comprising the antibody [0056]. Because the claims broadly recite any antibody binding to any region within an MGFR domain of a MUC1 protein inclusive of the PSMGFR domain and the specification defines these domains as extracellular domains, and Kufe teach such antibodies, the claims are anticipated by the prior art. Because Claims 5 and 6 recite comprising language of "up to X" modifications to the sequence of SEQ ID NO:36, which corresponds to the peptide sequence for the extracellular domain of Muc-1 described in Wreschner, the claims are considered to encompass an antibody binding to an unmodified sequence for the extracellular (SEQ ID NO:36 (native PSMGFR)), where zero modifications are read into the range.

Wreschner's disclosure for making monoclonal antibodies is explicit. Wreschner's disclosure for making monovalent antibodies is explicit. Applicants' argument that Wreschner does not appreciate the difference(s) between monovalent and bivalent antibodies is irrelevant and gratuitous because none of the instant claims are drawn to a bivalent antibody. The rejection is maintained."

The rejection was maintained in the Office Action of 6/15/10 as follows:

"Applicants' allegations on pp. 6-7 of the Response of 11/10/09 have been considered but are not found persuasive. Applicants allege Wreschner '324 discloses that its antibody was preferably made against the sequence located in the 15 amino acid sequence that resides at the N-terminal portion of the 59 amino acid segment. This 15 amino acid sequence includes SVVVQLTLAFREGTI. However, only the final "GTI" overlaps with the PSMGFR sequence of the claimed invention. Accordingly, it is believed that the Wreschner '324 antibody lies outside the scope of the antibody of the claimed invention.

Response to Arguments

The examiner respectfully submits that Applicants have not established by a preponderance of the evidence that the epitope for the monovalent antibody of Wreschner would not comprise or be overlapping with the final "GTI"

residues of the PSMGFR sequence. Also Wreschner teaches examples of monoclonal antibodies binding within this region and having the property of growth inhibition of MCF7 breast cancer cells.

The claimed antibody appears to be the same as the prior art antibodies, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989)."

The rejection was maintained in the Office Action of 7/5/11 as follows:

"Applicants allegations on pp. 5-6 of the Response of 6/15/10 have been considered and are not found persuasive. Applicants allege Wreschner '324 discloses that its antibody was preferably made against the 15 amino acid sequence SVVVQLTLAFREGTI. Since only the final "GTI" overlaps with the PSMGFR sequence of the claimed invention, the Wreschner '324 antibody lies outside the scope.

Response to Arguments

a) Applicants have not disclosed the epitope for the inventive antibody. Applicants have disclosed the sequence of SEQ ID NO:36 as comprising the binding site for the inventive antibody. Applicants make the bald face assertion that because 12 residues of Wreschner '324 lies outside the claimed range and 3 residues of Wreschner '324 fall within the range, that Wreschner '324 is not effective art. No where have Applicants shown which amino acid residues of the sequence are critical for antibody binding. No where have Applicants shown that the "GIT" region of the sequence is excluded from antibody binding. Applicants attorney arguments are unsubstantiated by any evidence. If Applicants wish to maintain this same position, then they are requested to provide data showing that the "GIT" residues are not critical for binding, and are otherwise excluded from the claim scope for the antibody.

MPEP 2144.05 ("Optimization of Ranges') states in part:

"Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.)."

b) Wreschner '324 discloses at [0049] that antibody fragments can be bispecific single chain Fv dimers (PCT/US92/09965) and (ix) "diabodies", multivalent or multispecific fragments constructed by gene fusion. The meaning of the embodiments is considered to represent a bivalent antibody of the instant claims."

Applicants allegations on pp. 5-6 of the Response of 7/5/11 have been considered and not found persuasive. Applicants allege Wreschner '324 discloses that its antibody was preferably made against the sequence located in the 15 amino acid sequence that resides at the N-terminal portion of the 59 amino acid segment. This 15 amino acid sequence includes SVVVQLTLAFREGTI. However, only the final "GTI" overlaps with the PSMGFR sequence of the claimed invention. Accordingly, it is

believed that the Wreschner '324 antibody lies outside the scope of the antibody of the claimed invention.

Response to Arguments

Applicants attorney arguments that "GTI" cannot be and is not immunogenic is opinion based and not fact based (MPEP 716.019(c) and 2145 "The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness.").

In addition, the claims are not limited to being monoclonal or polyclonal. Wreschner teaches making immunologically reactive antibodies to including polyclonal and monoclonal antibodies. The polyclonal antibodies are polyreactive and because of the extensive heterogeneity of the polyclonal population and the indefinite breadth of scope for the antibody of the instant claims, the claimed antibody appears to be the same as the prior art antibody, absent a showing of unobvious differences. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Finally, it is accepted in the art that an antibody epitope can be as small as three (3) amino acids. For example, see the attached data sheet from ImmunoGlobe GmbH

website (pp.1-3; 9/14/11) on selection of epitopes being as small as three residues against which antibodies can be made. Accordingly, there is no reason to believe or doubt that Wreschner's "GTI" region can be an epitope overlapping with the instant claimed sequence.

The rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. The rejection of Claims 17 and 199 under 35 U.S.C. 103(a) as being unpatentable over Wreschner et al. (US 20050019324; published 1/27/05; filed 3/26/02; cited in the PTO 892 form of 1/31/08) in view of Kufe et al. (WO 02/22685; published 3/21/02; filed 12/11/01; cited in the PTO 892 form of 1/31/08) is maintained.

The rejection was set forth in the Office Action of 1/3/11 as follows:

"Claims 17 and 199 are drawn to kits comprising the monovalent or bivalent antibody recognizing the sequence of SEQ ID NO: 36.

The claimed kits were prima facie obvious at the time of the invention.

Wreschner discloses an isolated antibody or fragment including monovalent and bivalent antibodies and fragments [0034; 0047], which specifically binds to an epitope in the extracellular region of an isoform of MUC1 protein [0019] where the epitope is located in the 15 amino acid sequence that resides at the N-terminal portion of the 59 amino acid segment which is located directly N-terminal to the transmembrane domain of the MUC1/Y, MUC1/X and MUC1/REP proteins [0044], a pharmaceutical composition comprising the antibody [0056]. The claims are considered to encompass an antibody binding to an unmodified sequence for the extracellular (SEQ ID NO:36 (native PSMGFR). Kufe appreciates compositions for administering as therapies or as diagnostics but does not disclose a kit comprising the anti-MGFR antibody as does Kufe.

Kufe discloses on p. 2, line 16 an extracellular domain of MUC-1 protein comprising amino acid residues corresponding to SEQ ID NO:36 for the PSMGFR domain, antibodies against the PSMGFR domain in both monovalent and bivalent forms (pp. 10-14; p. 31), and pharmaceutical compositions (p. 26-29). Because the claims recite any antibody binding to the PSMGFR domain, and Kufe teach such antibodies, the claims are anticipated by the prior art. Kufe teaches preparing the antibodies in vials for administration which would be encompassed as elements within a kit.

It would have been prima facie obvious to have produced a kit comprising the antibody of the invention and one would have been reasonably assured of success in having done so at the time of the invention based on Wreschner and Kufe. Both Wreschner and Kufe disclose antibodies recognizing the sequence TINVHDVETQFNQYKTEAASRYNLTISDVSVSDVPFPFSAQSGAG found in the extracellular domain of MUC1 protein. Both Wreschner and Kufe disclose compositions comprising the antibody for detecting the region of interest on the MUC1 protein, where such detection methods would have provided motivation to formulate the antibody into a kit. Specifically, Kufe teaches antibodies in vials, and therefore one of skill in the art would have been reasonably assured of success in having produced a kit for the antibody of the invention because kit/antibody combinations had been contemplated in the art at the time of the invention. For these reasons the kit comprising the anti-MGFR antibody or a binding fragment thereof would have been prima facie obvious."

Applicants allegations on p. 7 of the Response of 7/5/11 have been considered and not found persuasive. Applicants allege in view that Wreschner '324 is fails to disclose or suggest the presently claimed invention, as discussed above, it is believed that Kufe '685 fails to remedy this defect.

Response to Arguments

Applicants attorney arguments that "GTI" cannot be and is not immunogenic is opinion based and not fact based (MPEP 716.019(c) and 2145 "The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just

attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness.").

In addition, the claims are not limited to being monoclonal or polyclonal. Wreschner teaches making immunologically reactive antibodies to including polyclonal and monoclonal antibodies. The polyclonal antibodies are polyreactive and because of the extensive heterogeneity of the polyclonal population and the indefinite breadth of scope for the antibody of the instant claims, the claimed antibody appears to be the same as the prior art antibody, absent a showing of unobvious differences. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

It is accepted in the art that an antibody epitope can be as small as three (3) amino acids. For example, see the attached data sheet from ImmunoGlobe GmbH website (pp.1-3; 9/14/11) on selection of epitopes being as small as three residues against which antibodies can be made. Accordingly, there is no reason to believe or doubt that Wreschner's "GTI" region can be an epitope overlapping with the instant claimed sequence.

In view of the claims being anticipated by Wreschner for the antibody against the PSMGFR sequence, and further in view of Kufe disclosing antibodies recognizing the sequence TINVHDVETQFNQYKTEAASRYNLTISDVSVSDVPFPFSAQSGAG found in the extracellular domain of MUC1 protein and compositions and kits thereof, the

obviousness rejection is maintained..

The rejection is maintained.

Conclusion

11. No claims are allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Misook Yu can be reached on 571-272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lynn A. Bristol/
Primary Examiner, Art Unit 1643